REMARKS

Each rejection raised by the Examiner is addressed separately below. In view of the claim amendments noted above, the remarks discussed below, the concurrently filed § 1.132 Declaration of Dr. Gary Dahl (hereafter "Declaration"), and the concurrently filed Request for Continued Examination, Applicants respectfully request reconsideration of the merits of this patent application.

IN THE SPECIFICATION

The specification was amended to clarify that the *Bst* strains useful in the present application include ATCC number 12980 and 12016, both obtained from the American Type Culture Collection, in Rockville, Maryland. This amendment is merely a correction and clarification of the proper ATCC numbers of *Bst* strains useful in the present invention. No new matter is added.

IN THE CLAIMS

Claims 60, 61, 63, 64, 66, 67 and 71-74 are pending in this application. Claims 60 and 61 are currently amended for clarification and to restrict the claims to specific strains, as explained in the response below. Claims 71-74 are new dependent claims that are supported by the specification as filed. No new matter which is not in the specification has been added.

CLAIM REJECTIONS - 35 USC § 103

Claims 60, 61, 63, 64, 66 and 67 are rejected under 35 U.S.C. 103(a) as being unpatentable over Roche Molecular Biochemicals Catalog, 1999, pages 50-51; Sellman et al. Journal of Bacteriology, Vol 174, No. 13, pages 4350-4355; and Lu et al. BioFeedback, Vol 11, No. 4, pages 464-466, 1991.

The Applicant understands that the primary basis for the Examiner's rejection is that the Roche Molecular Biochemicals Catalog (1999) teaches that *Carboxydothermus hydrogenoformans* DNA polymerase has magnesium-dependent reverse transcriptase activity,

and therefore, it would have been obvious for the present Applicant to test for the reverse transcriptase activity of Bst DNA polymerase in the presence of magnesium ions and in the absence of manganese ions and the expectation of success was high. The Examiner acknowledged the Applicant's arguments that this was not obvious, but did not find Applicant's arguments persuasive. The Examiner went on to state (at the top of page 8 of the Examiner's September 28th, 2009 Office Action) that "the substitution of the Bst DNA polymerases taught by Sellman et al. or Lu et al. into the methods taught by Roche Molecular Biochemicals Catalog, 1999 would yield predictable results."

In order to determine if the latter statement of the Examiner that substitution of a DNA polymerase from a moderate thermophile, such as a DNA polymerase from any strain of Bst DNA polymerase or similar DNA polymerase would yield predictable results, meaning that the DNA polymerase would have reverse transcriptase activity in the presence of magnesium ions in the absence of manganese ions, the Applicant requested other scientific colleagues in the R&D Department of Applicant's employer to test three other commercially available DNA polymerases derived from similar moderately thermophilic bacteria for their respective reverse transcriptase activities (Declaration, paragraph 5). The three DNA polymerases chosen were:

(1) Bst DNA polymerase Large Fragment from New England BioLabs, Catalog Number: M0275M;

(2) BcaBEST™ DNA polymerase from Takara Bio Inc. The enzyme used was from the BcaBEST™ RNA PCR Kit Ver.1.1, Catalog Number: RR023A; and

(3) DisplaceAce™ DNA polymerase from EPICENTRE Biotechnologies. This is a truncated DNA polymerase derived from *Geobacillus kaustophilus.* Catalog Number: D08061K.

The reverse transcriptase activities of each of the three enzymes were assayed using methods similar to those described in the present application: (1) in the presence of manganese cations; and (2) in the presence of magnesium cations in the absence of manganese cations. Briefly, each of the tested DNA polymerases was incubated for 30 minutes at temperatures between 40-60 degrees C in a reverse transcription reaction mixture containing an RNA template, a primer complementary to the 3'-end of the template, all 4 deoxyribonucleoside triphosphates, and either only Mn^{2+} cations or only Mg^{2+} cations. Then, an aliquot of each reverse transcription reaction mixture was analyzed for the presence or absence of a first-strand cDNA band by electrophoresis on a denaturing agarose gel and staining the gel with SYBR® Gold dye to visualize the bands. (Declaration, para. 6).

Results of the reverse transcriptase assays were as shown in the following table (Declaration, para. 7):

Enzyme	**Source**	**cDNA Band Synthesized in Presence of Only:**	
		Magnesium	**Manganese**
Bst DNA Polymerase Large Fragment	New England BioLabs	NO	YES
BcaBest™ DNA Polymerase	Takara Bio Inc.	YES	YES
DisplaceAce™ DNA polymerase	EPICENTRE Biotechnologies	NO	YES

These results demonstrate very clearly that the substitution of the Bst DNA polymerases taught by Sellman et al. or Lu et al. into the methods taught by Roche Molecular Biochemicals Catalog, 1999 did not yield the predictable reverse transcriptase activity in the presence of only Mg^{2+} cations, as alleged by the Examiner. As shown in the table, although all of the commercially available DNA polymerases tested had reverse transcriptase activity in the presence of Mn^{2+} cations, only one of the three DNA polymerases had reverse transcriptase

activity in the presence of only Mg^{2+} cations in the absence of Mn^{2+} cations. (Declaration, para. 8).

In particular, although the presently pending application disclosed DNA polymerases from two Bst strains which had reverse transcriptase activity in the presence of only Mg^{2+} cations, the commercially available Bst DNA polymerase large fragment from New England Biolabs did not show activity in synthesizing a cDNA band that could be visualized on a gel in these assays. Thus, it is very clear from these experiments that it is not obvious that one of skill could substitute the Bst polymerases of Sellman or Lu into the methods of Roche with any predictable chance of success. Further, these results show that it is not obvious which Bst DNA polymerases will have reverse trancriptase activity in the presence of Mg^{2+} cations and in the absence of Mn^{2+} cations. The results also teach that the presently claimed methods are specific to the cited Bst polymerases from particular strains of bacteria and that this activity cannot even be predicted to be present in DNA polymerases from all bacterial strains comprising of a single genus and species category (e.g., all Bst strains), at least based on current categories of bacterial nomenclature.

Accordingly, to move prosecution forward, Applicant has amended Claims 60 and 61 to limit the claimed methods to only those DNA polymerases from particular bacterial strains which the Applicant identified as having the claimed activity.

The Applicant would also like to point out that the priority date for the present application goes back to a U.S. provisional patent application which was filed on May 22nd, 1999, and prior to that the assignee and employer of the present Applicant sold a Bst DNA polymerase large fragment, including for use in reverse transcription in the presence of Mg^{2+} cations and in the absence of Mn^{2+} cations, in 1999. Like the *Carboxydothermus hydrogenoformans* DNA polymerase, which was listed in the Roche Molecular Biochemicals 1999 Catalog, the Bst DNA polymerase large fragment product was listed in EPICENTRE's 1999/2000 catalog, a copy of which catalog product page is attached as Exhibit A. The EPICENTRE catalog page discloses that this product "has thermostable RNA-dependent (i.e., reverse transcriptase) activity", lists an application of the product as "First-strand cDNA

synthesis from primed RNA templates", and shows that the product provided a 10X Reaction Buffer that contained $MgCl_2$, but did not provide any source of Mn^{2+} cations." Thus, even without considering the additional information provided above, the Applicant believes that the product listing in the Roche Molecular Biochemicals 1999 Catalog does not provide a basis for rejecting the claims of the present application.

Still further, Applicants note that granted U.S. Patent Nos. 6,436,677, 7,094,539, and 7,504,220 all have claims similar to the present application, even though those applications were filed after the present application.

In view of the above arguments, Applicants request the Examiner to kindly withdraw the objections and allow the claims.

CONCLUSION

The application is believed to be in condition for allowance and allowance of the same is requested. If all the claims are not allowed, Applicant requests a telephone interview with the Examiner and his supervisor. The Commissioner is authorized to charge any fees under 37 CFR § 1.17 that may be due on this application to Deposit Account 17-0055. Applicants have enclosed a Petition for Two Month Extension of Time and a Request for Continued Examination. If further fees are necessary, please charge Deposit Account 17-0055. The Commissioner is also authorized to treat this amendment and any future reply in this matter requiring a petition for an extension of time as incorporating a petition for extension of time for the appropriate length of time as provided by 37 CFR § 136(a)(3).

Respectfully submitted,

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/Ann E. Rabe/

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